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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/396,985	09/15/99	BEUTLER	

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HM12/0801

EXAMINER
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BASI, N

ART UNIT	PAPER NUMBER
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1646

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DATE MAILED: 08/01/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/396,985

Applicant(s)

BEUTLER ET AL

Examiner

Nirmal. S. Basi

Group Art Unit

1646

☒ Responsive to communication(s) filed on Apr 18, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 38-40 and 52-99 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 38-40 and 52-99 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 8

☒ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### **DETAILED ACTION**

1. Amendment and Response to Restriction requirement filed 4/18/00 has been entered.

#### ***Election/Restriction***

2. Applicant's election with traverse of group IV, claims 38-40 in Paper No. 9 is acknowledged.

5 Since Applicant has canceled all non-elected groups the traversal of the claims is moot.

The requirement is still deemed proper and is therefore made FINAL.

#### ***Specification***

3. The disclosure is objected to because of the following informalities:

10 The drawings objected to because each Figure must described separately in the Brief Description of the Drawings. FIG. 7A is contained on two separate sheets. FIG. 7A must be labeled as FIG. 7A and FIG. 7B and described in the Brief Description of the Drawings as FIGS. 7A-7B or the equivalent, as required by 37 C.F.R. § 1.84 (u)(1). FIG 7B must be labeled as FIG. 7C. Appropriate correction is required.

- 15 4. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in FIG. 7, FIG. 14 must  
20 be identified by their corresponding SEQ ID NO:.

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**Claim Rejection, 35 U.S.C. 112, second paragraph**

5. Claims 38-40 and 52-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5           Claims 38 and 77 are indefinite because the name TLR-4 has not been defined in the claims and specification so as to allow the metes and bounds of the claims to be determined. The name TLR-4 polypeptide is not an art accepted term and does not provide any structural or functional properties of the polypeptide. It is suggested that TLR-4 polypeptide be identified by its SEQ ID NO:.. Further for clarity it is suggested that LPS be given its full name, lipopolysaccharide. Further, 10       claim 38 is indefinite because the method steps do not achieve the goal of screening for modulators of an LPS mediated response as stated in the preamble. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved (the method does not contain an assay step which states how and when the goal of the claim is achieved). In claim 77 it is not clear 15       how the “change in the activity of TLR-4 polypeptide contacted with the candidate substance is related to the standard activity profile” to indicate that the candidate compound substance is a modulator of LPS mediated response. Also claims 38 and 77 are indefinite because it is not clear what is a “standard activity profile”, what it measures and how it is assayed so as to allow the metes and bounds of the claim to be determined. Further it is not clear what LPS mediated response is 20       measured or what method steps are used to obtain a TLR- polypeptide.

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Claims 40 and 78 are indefinite because it is not clear what is the reporter gene, what said gene reports and what is the promotor from a TLR-4 gene so as to allow the metes and bounds of the claim to be determined.

5        Claims 40 and 78 is indefinite because it is not clear what is a "standard activity profile", what it measures and how it is assayed so as to allow the metes and bounds of the claim to be determined.

Claims 52 and 79 are indefinite because it is not clear what "function" of TLR-4 is affected.

Claims 52, 55, 56, 62-64, 76, 79, 82, 83, 86, 87 and 99 are indefinite because it is not clear what is a TLR-4. "TLR-4" is indefinite for reasons given above.

10        Claim 62 and 85 are indefinite because it is not clear what are the "conditions that normally allow for TLR-4 transcription and translation" so as to allow the metes and bounds of the claim to be determined.

Claims 69 and 92 are indefinite because it is not clear what is a, "small molecule inhibitor", so as to allow the metes and bounds of the claim to be determined. What small molecule is being inhibited?

15        Claim 71 is indefinite because "stimulator of an immune response" does not provide any structural limitations to the modulator so as to allow the metes and bounds of the claim to be determined.

20        Claims 76 and 99 are indefinite because it is not clear what knowledge of the TLR-4 protein structure would allow for the selection of a putative modulator or what structure said modulator would have so as to allow the metes and bounds of the claim to be determined

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Claim 85 recites the limitation "said nucleic acid segment" in claim 77. There is insufficient antecedent basis for this limitation in the claim.

Claim 62 recites the limitation "said nucleic acid segment" in claim 38. There is insufficient antecedent basis for this limitation in the claim.

5            Claims 90 and 67 contain an improper Markush grouping because it refers to both sources of living material and marine samples which may non living.

Claims 39, 53-5, 57-61, 65, 66, , 68-70, 71-75, 80-81, 84-88, 89, 91, 93-98 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

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**Claim Rejection, 35 U.S.C. 112**

6.        Claims 38-40 and 52-99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a screening method for compounds which modulate a LPS mediated response by inducing the synthesis or altering the activity of TLR-4 of SEQ ID NOs: 2, 4, 6, 98 and 99, does not reasonably provide enablement for other methods of screening for  
15        compounds which may affect any other LPS-mediated responses or methods for identification of compounds which may predictably have other activities by any way other means than the altered expression of TLR-4 (SEQ ID Nos:2, 4, 6, 98 and 99). The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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The claims are directed to screening for modulators of a LPS mediated response. The specification discloses that TLR-4 mRNA is induced by LPS (Fig 9) and TLR4 is the limiting factor in LPS signal transduction in LPS responsive macrophages, the quantity of TLR4 expressed is an important limiting factor in the intensity of the signal that is evoked (page 128). The specification discloses the screening of modulators of LPS mediated response where the compounds screened can modulate the expression of TLR-4 of SEQ ID NOs:2, 4, 6, 98 and 99. The scope of the claims which encompasses other methods of screening for modulators of LPS, using proteins other than those disclosed in SEQ ID NOs:2, 4, 6, 98 and 99, where the compounds may have activity by other means than the altered expression of TLR-4 expression of SEQ ID NOs:2, 4, 6, 98 and 99 is not enabled by the disclosure.. For the person of ordinary skill in the art to screen for modulators of a LPS mediated response by any other means than those disclosed as “enabling” above, the artisan must first isolate other proteins capable of direct or indirect interaction with LPS and its modulators, and develop screening assays to determine if certain compounds can be modulators of the LPS mediated response. Therefore, the lack of guidance provided in the specification as to what other assays may be used to screen for modulators of LPS, unpredictability and undue experimentation in isolating other TLR-4 polypeptides would prevent the skilled artisan from practicing the invention in its full scope.

No claim is allowed

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**Advisory Information**


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi  
Art Unit 1646  
July 31, 2000

  
**YVONNE EYLER, PH.D**  
**PRIMARY EXAMINER**